Infrainguinal bypass is associated with lower perioperative mortality than major amputation in high-risk surgical candidates

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Background: **Major amputation is often selected over infrainguinal bypass in patients with severe systemic comorbidities because it is assumed to have lower perioperative risks, yet this assumption is unproven and largely unexamined.**
Methods: **The 2005 to 2008 National Surgical Quality Improvement Project (NSQIP) database was used to identify all patients undergoing either infrainguinal bypass or major amputation using procedural codes. Patients with systemic or local infections were excluded. A subset of high-risk patients were then defined as American Society of Anesthesiologists (ASA) class 4 or 5, or ASA class 3 with renal failure, dyspnea at rest, ventilator dependence, recent congestive heart failure, or recent myocardial infarct. Propensity score matching was used to obtain two high-risk patient groups matched for preoperative characteristics.**
Results: **No significant differences in demographic, preoperative, or anesthetic variables were found between the matched, high-risk amputation or bypass groups (792 and 780 patients, respectively). Bypass was associated with a lower 30-day postoperative mortality than amputation (6.54% vs 9.97%; $P = .0147$). Amputation was associated with higher rates of pulmonary embolism (0.9% vs 0% for amputation vs bypass groups, respectively; $P = .009$) and urinary tract infection (5.2% vs 2.7%; $P = .01$), while bypass was associated with higher rates of return to the operating room (14.1% vs 27.6%; $P < .001$) and a trend toward higher postoperative transfusion requirements (0.9% vs 2.1%; $P = .054$). The postoperative time to discharge did not differ between the two groups.**
Conclusion: **The decision to perform an infrainguinal bypass or amputation should depend on well-established predictors of graft patency and functional success rather than presumptions about different perioperative risks between the two procedures. (J Vasc Surg 2011;53:1251-9.)**

Peripheral arterial disease affects approximately 5 million people in the United States. Non-Hispanic blacks, diabetics, and the elderly seem disproportionately affected, with prevalence rates of 7.9%, 10.8%, and 14.5% in these groups, respectively. With an increasing incidence of diabetes mellitus and increasing numbers of elderly patients, the prevalence of peripheral arterial disease is expected to increase as well.[1] For patients with critical limb ischemia due to lower extremity (ie, infrainguinal) occlusive disease, open revascularization remains the most effective means of achieving limb salvage. Lower extremity revascularization can achieve limb salvage (preservation of the foot allowing ambulation without a prosthetic[2]) in 88% of patients,[3] and meta-analysis of three major randomized trials of infrainguinal bypass had a mortality rate of 2.7%.[4] Furthermore, there is some evidence that a successful attempt at revascularization may be associated with lower hospital costs than primary amputation.[5]

Lower extremity amputation, on the other hand, is typically reserved for patients who are considered poor bypass candidates for a host of reasons, including inadequate distal target vessels, failed previous attempts at revascularization, poor functional status, or the presence of multiple severe medical comorbidities.[6] Indeed, of the 300,000 patients in the United States that present each year with critical limb ischemia, approximately 25% will undergo amputation without an attempt at revascularization. Estimates of the perioperative mortality rate for major amputation (defined as any amputation that does not preserve at least part of the foot) range from 6% to 17%.[7-10] While this high rate is often attributed to the presence of multiple severe systemic comorbidities,[1,11] a risk-adjusted comparison of the perioperative mortality and morbidity of infrainguinal bypass and major amputation has not been done.

The objective of the current study was to perform a risk-adjusted comparison of the early (30 day) postoperative morbidity and mortality of infrainguinal bypass with major amputation in a patient population with multiple severe, systemic comorbidities to determine if primary amputation would indeed offer a survival benefit among high-risk patients.

METHODS

Study subjects. This study represents a retrospective cohort study based on the American College of Surgeons

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Conflicts of interest: none.
Additional material for this article may be found online at www.jvascsurg.org.
Presented at the 2010 Vascular Annual Meeting of the Society for Vascular Surgery, Boston, Mass, June 10-13, 2010.

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The editors and reviewers of this article have no relevant financial relationships to disclose per the JVS policy that requires reviewers to decline review of any manuscript for which they may have a competition of interest.
0741-5214/$36.00

doi:10.1016/j.jvs.2010.11.099

National Surgical Quality Improvement Project (NSQIP) database from private sector (ie, non-Veteran's Administration) hospitals. Data from the 2005 to 2008 NSQIP database were used to identify patients that underwent infrainguinal bypass (using prosthetic or autologous conduit) and patients that underwent major amputation (defined as above-knee or below-knee amputation). These were identified based on Common Procedural Terminology codes (Appendix, online only). This study was approved by the Partners Human Research Committee under Protocol #2009-P-002571/1.

Our ultimate goal was to identify two comparable cohorts of patients who had undergone infrainguinal bypass or major lower extremity amputation but who might be considered candidates for either procedure. To avoid inclusion of patients who would have had a strong contraindication toward revascularization attempts because of wet gangrene (and thus were candidates only for major amputation), we excluded all patients categorized as having preoperative bacteremia, sepsis, or septic shock, or any patient whose operative site was classified as infected or dirty.

Next, a subset of high-risk patients was identified. Criteria to define high-risk surgical candidates consisted of the following:

- Any patient that was classified as American Society of Anesthesiologists Physical Status Classification 4 (ASA 4, severe systemic disease that is a constant threat to life) or ASA 5 (a moribund patient who is not expected to survive without the operation).[12]
- Any patient classified as ASA 3 (a patient with severe systemic disease) was included if one or more of the following was also present: congestive heart failure exacerbation within the past 30 days; myocardial infarct within the past 6 months; history of angina within 30 days of surgery; dyspnea at rest; mechanical ventilator dependence before the operation; or renal failure (serum creatinine >3.0 mg/dL, or dialysis dependence).

Secondary analysis was performed using a subset of the above-described high-risk study group. This subset included only patients classified as having gangrene or rest pain and excluded patients with complete functional dependence (ie, no ability to independently perform activities of daily living), and/or those classified as ASA 5. Propensity scoring was again used to obtain two groups matched for demographic, preoperative, and perioperative characteristics, and again yielded two comparable groups lacking in significant or important differences.

Propensity matching. A nonparsimonious logistic regression analysis model was created to estimate the likelihood of undergoing amputation or infrainguinal bypass given various preoperative clinical and demographic characteristics. The model was created using backward stepwise regression using a $P = .05$ level. A propensity score was then created from the final model and used to stratify patients into quintiles. A random subset of patients were selected from each of the five stratum, as according to Rubin,[13] to create two propensity-matched groups with similar preoperative characteristics and differing only by the treatment option the subject underwent.

Statistical analysis. Survival was estimated using the Kaplan-Meier product-limit estimate, and comparisons between survival functions were made with the log-rank test. Group differences were further compared using the χ^2 test for categorical variables and the nonparametric Mann–Whitney U test for continuous variables. Time from operation to discharge was analyzed using Kaplan-Meier estimates; deaths within 30 days of the operation were counted as censored observations. SPSS version 11.0 (SPSS Corporation, Chicago, Ill) and Intercooled Stata version 8.2 (StataCorp, College Station, Tex) were used for all statistical analyses and graphing. A P value of $< .05$ was considered statistically significant.

RESULTS

Baseline characteristics of patients undergoing amputation and bypass. Between 2005 and 2008, a total of 1105 patients who underwent major amputation and 1943 who underwent infrainguinal bypass met the defined criteria to be considered high-risk. These patients differed significantly in many characteristics; these characteristics are summarized in Table I. Compared to the infrainguinal bypass patients, major amputation patients were more likely to have had do-not-resuscitate orders (9.1% vs 1.7% for the amputation vs bypass groups, respectively; $P < .0001$), regional anesthesia (19.1% vs 10.4%, respectively; $P < .001$), insulin-dependent diabetes mellitus (52.0% vs 33.5%, respectively; $P < .001$), history of cerebrovascular accident with residual defect (19.1% vs 10.6%; $P < .001$), and pneumonia (3.1% vs 0.9%, respectively; $P < .001$). Amputation patients were less likely to have had previous percutaneous coronary intervention (18.4% vs 26.1%; $P < .001$), previous cardiac surgery (31.2% vs 37.4%, respectively; $P < .001$), or non-insulin-dependent diabetes (13.8% vs 21.1%, respectively; $P < .001$). Finally, patients who had major amputations were more often of African American descent than patients who had infrainguinal bypass (25.1% vs 19.2%, respectively; $P < .001$). Other statistically significant differences with smaller absolute differences in prevalence are listed in Table I. The 30-day survival rates were 88.29% for the nonmatched high-risk amputation group and 94.85% for the nonmatched high-risk bypass group ($P < .0001$).

Baseline characteristics of propensity-matched cohorts. Propensity matching resulted in two matched cohorts containing 792 patients who had a major amputation and 781 patients who had an infrainguinal bypass. Baseline characteristics for these patients did not differ significantly in any of the 36 variables listed in Table II. Of the patients in the major amputation group, 366 (46.2%) underwent above-knee amputations and 426 (53.8%) underwent below-knee amputations. Of the patients in the infrainguinal bypass group, 366 patients (46.9%) underwent femoropopliteal bypass, 322 patients (41.3%) underwent femorotibial or femoroperoneal bypass, and 92 pa-

Table I. Comparison of demographic and preoperative characteristics for nonstratified high-risk amputation (n = 1105) and bypass (n = 1943) patients

Variable	*Amputation group No. (%)*	*Bypass group No. (%)*	P *value*
Age			
<65 years old	387 (35.1)	624 (32.1)	.09
65-74 years old	292 (26.5)	582 (29.9)	.04[a]
75-89 years old	377 (34.2)	691 (35.5)	.45
90 + years old	46 (4.2)	46 (2.3)	.005[b]
Race/ethnicity			
White	692 (62.8)	1322 (68.0)	.003[b]
African American	277 (25.1)	373 (19.2)	<.001[b]
Hispanic	59 (5.3)	111 (5.7)	.68
Asian, Native American, other	74 (6.7)	137 (7.1)	.73
Male gender	687 (62.3)	1213 (62.4)	.96
CHF within 30 days before operation	138 (12.5)	208 (10.7)	.13
MI within 6 months before operation	105 (9.5)	152 (7.8)	.10
Angina within 1 month before operation	30 (2.7)	90 (4.6)	.009[b]
Previous percutaneous coronary intervention	203 (18.4)	508 (26.1)	<.001[b]
Previous cardiac surgery	344 (31.2)	727 (37.4)	<.001[b]
Ventilator dependence, preoperatively	33 (3.0)	18 (0.9)	<.001
Dyspnea at rest	79 (7.2)	163 (8.4)	.23
History of severe COPD	192 (17.4)	401 (20.6)	.03[a]
Pneumonia	34 (3.1)	18 (0.9)	<.001[b]
Serum creatinine >3 mg/dL	357 (32.4)	500 (25.7)	<.001[b]
Dialysis	386 (35.0)	499 (25.7)	<.001[b]
Acute renal failure	52 (4.7)	87 (4.5)	.76
Non-insulin-dependent diabetes	152 (13.8)	410 (21.1)	<.001[b]
Insulin-dependent diabetes	573 (52.0)	651 (33.5)	<.001[b]
History of smoking within 1 year preoperatively	267 (24.2)	648 (33.3)	<.001[b]
History of CVA with residual deficit	211 (19.1)	206 (10.6)	<.001[b]
Partial or complete functional dependence before current illness	546 (49.0)	339 (17.4)	<.001[b]
DNR, preoperatively	100 (9.1)	33 (1.7)	<.0001[b]
Obese (BMI >30 kg/m^2)	292 (26.5)	498 (25.6)	.60
Chronic steroid use	83 (7.5)	111 (5.7)	.048[a]
Weight loss >10% during 6 months before operation	44 (4.0)	47 (2.4)	.014[b]
ASA classification			
ASA 3	254 (23.0)	542 (27.9)	.003[b]
ASA 4	833 (75.6)	1379 (70.9)	.006[b]
ASA 5	8 (0.7)	8 (0.4)	.25
ASA n + E	103 (9.3)	162 (8.3)	.34
Anesthetic technique			
General anesthesia	881 (79.9)	1720 (88.5)	<.001[b]
Regional anesthesia	210 (19.1)	202 (10.4)	<.001[b]

ASA, American Society of Anesthesiologists; *BMI,* body mass index; *CHF,* congestive heart failure; *COPD,* chronic obstructive pulmonary disease; *CVA,* cardiovascular accident; *DNR,* do not resuscitate; *MI,* myocardial infarction.
[a]$P < .05$.
[b]$P < .01$.

tients (11.8%) underwent distal origin graft creation (Table III shows further details). The median duration of anesthesia was 2 hours for major amputation and 4 hours 48 minutes for patients receiving infrainguinal bypass.

Perioperative morbidity and mortality of the propensity-matched cohorts. Comparison of the two groups demonstrated that infrainguinal bypass was associated with significantly better 30-day survival than major amputation in high-risk surgical candidates (93.46% vs 90.03%; P = .0147; Fig 1). Amputation was associated with significantly higher rates of pulmonary embolism (0.9% vs 0% for amputation vs bypass groups, respectively; P = .009) and urinary tract infection (5.2% vs 2.7%, respectively; P = .01), while bypass was associated with significantly higher rates of return to odds ratio (14.1% vs 27.6%, respectively; $P < .001$) and a trend toward higher bleeding events requiring transfusion (0.9% vs 2.1%, P = .054; Table IV). The median postoperative length of stay was 6 days for patients receiving amputation and 7 days for patients receiving bypass surgery. As demonstrated in Fig 2, there was no significant difference in the time from operation to discharge (P = .21).

Comparison of the critical limb ischemia subset. Propensity matching for the subset of patients denoted as having critical limb ischemia and excluding patients with complete functional dependence or that were classified as ASA 5 yielded 500 patients with major amputations and 505 patients with infrainguinal bypass. Again, baseline

Table II. Comparison of demographic and preoperative characteristics for high-risk amputation (n = 792) and bypass (n = 781) patients matched by propensity scoring

Variable	*Amputation group No. (%)*	*Bypass group No. (%)*	P *value*
Age			
<65 years old	286 (36.1)	278 (35.6)	.85
65-74 years old	212 (26.8)	209 (26.8)	.99
75-89 years old	272 (34.3)	271 (34.7)	.87
90 + years old	22 (2.8)	22 (2.8)	.96
Race/ethnicity			
White	507 (64.0)	488 (62.6)	.55
African American	189 (23.9)	187 (24.0)	.96
Hispanic	43 (5.4)	52 (6.7)	.30
Asian, Native American, other	53 (6.7)	53 (6.8)	.94
Male gender	493 (62.2)	489 (62.7)	.86
CHF within 30 days before operation	98 (12.4)	92 (11.8)	.73
MI within 6 months before operation	67 (8.5)	70 (9.0)	.72
Angina within 1 month before operation	26 (3.3)	18 (2.3)	.24
Previous PCI	164 (20.7)	159 (20.4)	.87
Previous cardiac surgery	269 (34.0)	259 (33.2)	.75
Ventilator dependence, preoperatively	18 (2.3)	16 (2.1)	.76
Dyspnea at rest	63 (8.0)	57 (7.3)	.63
History of severe COPD	142 (17.9)	142 (18.2)	.89
Current pneumonia, preoperatively	20 (2.5)	11 (1.4)	.11
Serum creatinine >3 mg/dL	248 (31.3)	250 (32.1)	.75
Dialysis	254 (32.1)	265 (34.0)	.45
Acute renal failure	37 (4.7)	34 (4.7)	.95
Non-insulin-dependent diabetes	127 (16.0)	136 (17.4)	.48
Insulin-dependent diabetes	370 (46.7)	358 (45.9)	.75
History of smoking within 1 year preoperatively	220 (27.8)	224 (28.7)	.68
History of CVA with residual deficit	127 (16.0)	107 (13.7)	.20
Partial or complete functional dependence before current illness	293 (37.0)	261 (33.5)	.14
DNR, preoperatively	37 (4.7)	27 (3.5)	.23
Obese (BMI >30 kg/m^2)	209 (26.4)	204 (26.2)	.92
Chronic steroid use	68 (8.6)	51 (6.5)	.13
Weight loss >10% during 6 months before operation	29 (3.7)	30 (3.8)	.85
ASA classification			
ASA 3	200 (25.5)	207 (26.5)	.56
ASA 4	581 (73.4)	569 (72.9)	.86
ASA 5	6 (0.8)	3 (0.4)	.32
ASA n + E	83 (10.5)	70 (9.0)	.31
Anesthetic technique			
General anesthesia	657 (82.9)	652 (83.5)	.74
Regional anesthesia	126 (15.9)	123 (15.8)	.94

ASA, American Society of Anesthesiologists; *BMI,* body mass index; *CHF,* congestive heart failure; *COPD,* chronic obstructive pulmonary disease; *CVA,* cardiovascular accident; *DNR,* do not resuscitate; *MI,* myocardial infarction; *PCI,* percutaneous coronary intervention.

Table III. Primary procedures performed in the high-risk, propensity score-matched infrainguinal bypass group (n = 780)

Procedure	*Vein conduit*	*PTFE conduit*	*Total*
Femoropopliteal bypass	182 (23.3%)	184 (23.6%)	366 (46.9%)
Femorotibial or femoroperoneal	245 (31.4%)	77 (9.9%)	322 (41.3%)
Distal origin grafts	83 (10.6%)	9 (1.2%)	92 (11.8%)
Total	507 (65.3%)	270 (34.6%)	780 (100%)

PTFE, Polytetrafluoroethylene.

characteristics for these patients did not differ significantly in any of 36 variables (Table V). Comparison of these two groups demonstrated 30-day survival rates that were nearly identical to that of the larger propensity-matched high-risk study group, with a trend toward better survival among the patients receiving bypass (93.86% vs 90.60%; P = .0557; Fig 3). The median postoperative length of stay was 6 days for both the patients who received amputation and those who had a bypass, and the time from operation to discharge did not differ significantly between the two groups (P = .2).

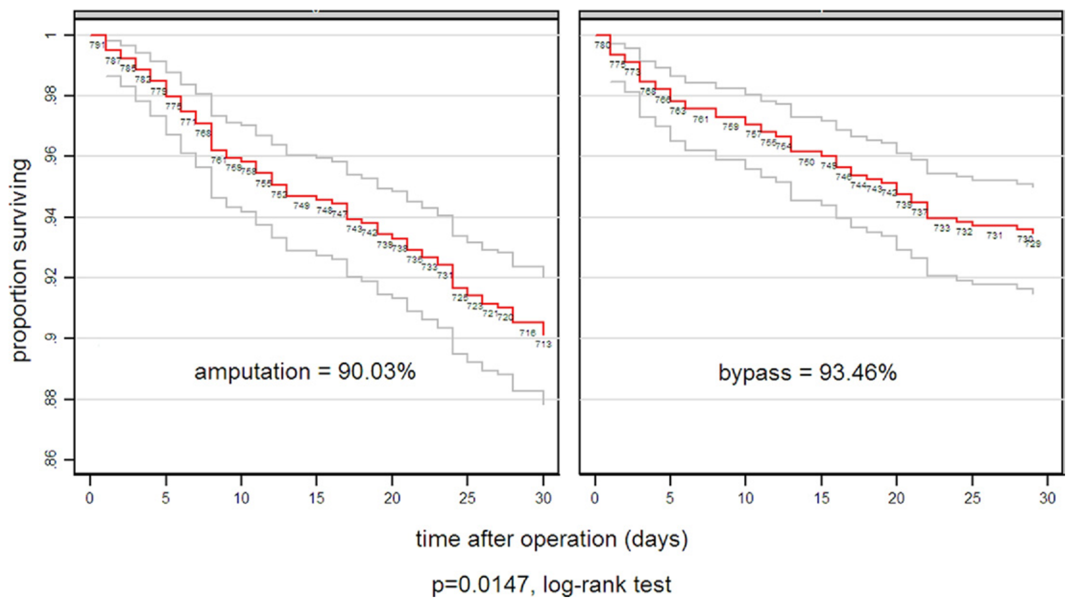

Fig 1. Kaplan-Meier product-limit estimate of 30-day postoperative mortality for high-risk, propensity score-matched patients undergoing major amputation (n = 792) or infrainguinal bypass (n = 780).

Table IV. A comparison of early postoperative events in the propensity-matched amputation and bypass cohorts

Variable	*Amputation group*	*Bypass group*	P *value*
Wound disruption	12 (1.5)	17 (2.2)	.33
Superficial surgical site infection	48 (6.1)	55 (7.1)	.43
Deep incisional surgical site infection	29 (3.7)	31 (4.0)	.75
Pneumonia	36 (4.5)	30 (3.8)	.49
Unplanned intubation	27 (3.4)	39 (5.0)	.12
Deep venous thrombus	11 (1.4)	9 (1.2)	.68
Pulmonary embolism	7 (0.9)	0 (0.0)	.009[b]
Mechanical ventilation for >48 hours	20 (2.5)	32 (4.1)	.08
Progressive renal insufficiency	8 (1.0)	9 (1.2)	.78
Acute renal failure	15 (1.9)	13 (1.7)	.73
Urinary tract infection	41 (5.2)	21 (2.7)	.01[a]
Cardiac arrest requiring cardiopulmonary resuscitation	15 (1.9)	22 (1.7)	.23
Myocardial infarction	8 (1.0)	9 (1.2)	.78
Bleeding requiring transfusion	7 (0.9)	16 (2.1)	.05[a]
Sepsis	43 (14.1)	44 (5.6)	.85
Septic shock	37 (4.7)	35 (4.5)	.86
Return to the operating room	112 (14.1)	215 (27.6)	<.001[b]

[a] $P < .05$.
[b] $P < .01$.

DISCUSSION

Patients deemed "high risk" because of the presence of systemic comorbidities are often excluded from being candidates for limb salvage through surgical revascularization and are instead offered major amputation.[8] Even among the dedicated vascular surgical centers participating in the Bypass versus Angioplasty in Severe Ischaemia of the Leg (BASIL) trial, for example, a "significant comorbidity precluding bypass surgery," excluded 7% of patients with critical and subcritical limb ischemia from enrollment and attempts at revascularization.[14] Is this a valid reason to exclude patients from revascularization attempts? The decision between offering a major amputation or an attempt at limb salvage through surgical revascularization is often quite challenging, but remains a fundamental role of the vascular surgeon in the care of patients with peripheral vascular disease. Fortunately, many of the other factors typically considered in the decision-making process are well studied, including the extent of foot necrosis,[15,16] location of the distal target,[17] the quality of outflow,[18] the availability of an adequate vein graft conduit,[19] and a patient's preoperative functional status and potential for postoperative ambulation[20-23] are factors that have been studied in thousands of patients over the course of several decades in

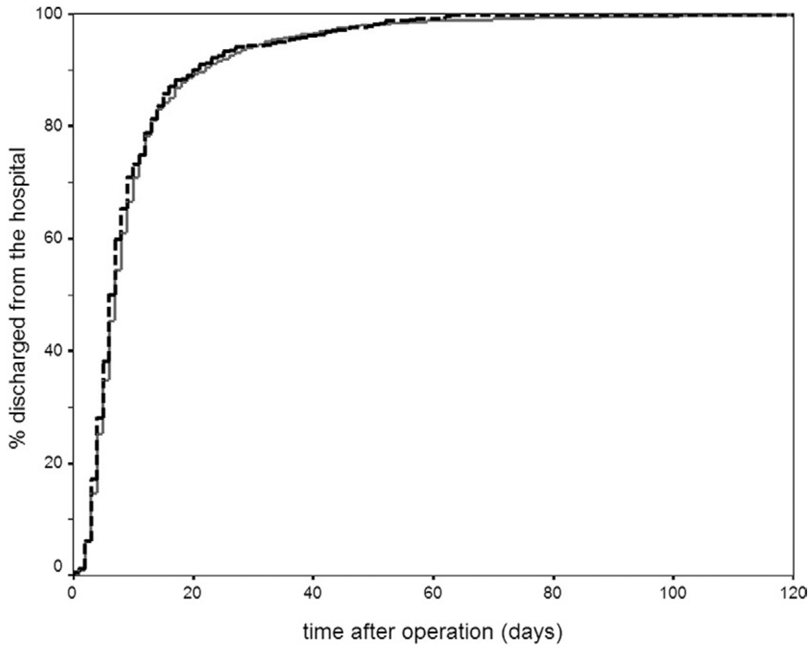

Fig 2. Kaplan-Meier product-limit estimate demonstrating time from operation to discharge for amputation patients (n = 792, *black broken line*) or infrainguinal bypass (n = 780, *solid gray line*).

both large single-center retrospective studies[24] and large multicenter prospective clinical trials,[3,25,26] and the impact of these factors on patency and limb salvage is well-documented. Our understanding of the relative perioperative safety (morbidity and mortality) of major amputation and infrainguinal bypass operations is largely based on retrospective analyses, but direct comparisons have been admittedly limited because of the nonrandomized, non-matched nature of the patient populations (ie, important and unadjusted differences in the baseline characteristics of the patient populations that undergo these operations). Much of the increased perioperative mortality associated with major amputation has been attributed to this population having a higher prevalence of major systemic comorbidities than the bypass population (rather than the procedure itself),[11] but this is an assumption that has remained unproven and largely unchallenged.

Our study attempts to examine this assumption and address the larger question of how systemic comorbidities might inform the amputation vs revascularization decision-making process. To accomplish this, we used propensity score matching to identify cohorts of high-risk patients undergoing major amputation and infrainguinal revascularization. An examination of Table II demonstrates that these two groups are indeed comparable and clearly supports their characterization as high risk. In the unmatched patient population, we found that the 30-day mortality among the major amputation and infrainguinal bypass groups were 11.71% and 5.15%, respectively, comparable to rates seen in large series detailing outcomes after these procedures.[3,8,14] In these risk-matched high-risk cohorts, however, we found that infrainguinal revascularization was not associated with higher 30-day mortality or major morbidity than major amputation. Indeed, there was a small but statistically significant survival benefit associated with infrainguinal bypass (93.46% vs 90.03%; $P = .015$). The overall incidence of major complications was similar but had a different distribution between the two groups: the rate of return to the operating room and the need for a blood transfusion was higher among the patients receiving bypass and the rate of urinary tract infections and pulmonary emboli (consistent with previous studies[27-30]) was higher in the amputation group. Since major amputation seems no safer than revascularization in these high-risk patients, the presence of severe systemic comorbidities alone should not preclude patients from an attempt at surgical revascularization. Instead, the decision between major amputation and limb salvage through surgical revascularization should be based on patient preference and the well-studied, influential factors mentioned above.

One limitation of the American College of Surgeons NSQIP data used in this study may be the variable that describes the presence of rest pain or tissue loss. Initial examination of this variable showed that only 68% of the patients that underwent major amputations by vascular surgeons had rest pain or tissue loss. Although not all amputations have rest pain or tissue loss as an indication (perhaps as many as 10% are done for reasons other than critical limb ischemia[9]), this surprisingly low number suggested to us that the variable may not perfectly identify all patients who had critical limb ischemia. To address this concern, we performed a subset analysis with only patients

Table V. Comparison of demographic and preoperative characteristics for high-risk amputation (n = 500) and bypass (n = 505) patients with critical limb ischemia matched by propensity scoring

Variable	*Amputation group No. (%)*	*Bypass group No. (%)*	P *value*
Age			
<65 years old	172 (34.4)	178 (35.2)	.829
65-74 years old	143 (28.6)	149 (29.5)	.752
75-89 years old	168 (33.6)	167 (33.1)	.858
90 + years old	17 (3.4)	11 (2.2)	.829
Race/ethnicity			
White	314 (62.8)	316 (62.6)	.948
African American	123 (24.6)	118 (23.4)	.647
Hispanic	26 (5.2)	35 (6.9)	.251
Asian, Native American, other	37 (7.4)	36 (7.1)	.868
Male gender	314 (62.8)	296 (58.6)	.174
CHF within 30 days before operation	52 (10.4)	58 (11.5)	.582
MI within 6 months before operation	43 (8.6)	40 (7.9)	.696
Angina within 1 month before operation	12 (2.4)	20 (4.0)	.159
Previous PCI	97 (19.4)	101 (20.0)	.811
Previous cardiac surgery	176 (35.2)	187 (37.0)	.546
Ventilator dependence, preoperatively	1 (0.2)	2 (0.4)	.569
Dyspnea at rest	40 (8.0)	40 (7.9)	.528
History of severe COPD	88 (17.6)	107 (21.2)	.150
Current pneumonia, preoperatively	8 (1.6)	7 (1.4)	.780
Serum creatinine >3 mg/dL	177 (35.4)	167 (33.1)	.436
Dialysis	181 (36.2)	175 (34.7)	.608
Acute renal failure	20 (4.0)	16 (3.2)	.478
Non-insulin-dependent diabetes	72 (14.4)	87 (17.2)	.219
Insulin-dependent diabetes	246 (49.2)	232 (45.9)	.301
History of smoking within 1 year preoperatively	136 (27.2)	15.2 (30.1)	.310
History of CVA with residual deficit	72 (14.4)	67 (13.3)	.603
Partial functional dependence before current illness	295 (59.0)	283 (56.0)	.342
DNR, preoperatively	25 (5.0)	15 (3.0)	.100
Obese (BMI >30 kg/m^2)	127 (25.4)	133 (26.3)	.735
Chronic steroid use	41 (8.2)	30 (5.9)	.162
Weight loss >10% during 6 months before operation	21 (4.2)	16 (3.2)	.385
ASA classification			
ASA 3	133 (26.6)	138 (27.3)	.851
ASA 4	367 (73.4)	367 (72.7)	.795
ASA 5	—	—	—
ASA n + E	39 (7.8)	40 (7.9)	.943
Anesthetic technique			
General anesthesia	402 (80.4)	417 (82.6)	.375
Regional anesthesia	93 (18.6)	81 (16.0)	.283

ASA, American Society of Anesthesiologists; *BMI,* body mass index; *CHF,* congestive heart failure; *COPD,* chronic obstructive pulmonary disease; *CVA,* cardiovascular accident; *DNR,* do not resuscitate; *MI,* myocardial infarction; *PCI,* percutaneous coronary intervention.

that were identified as having critical limb ischemia (in addition to excluding patients with complete functional dependence and those classified as ASA category 5). The results of this subset analysis were similar to those of the full analysis incorporating all high-risk patients, including nearly identical 30-day survival rates. We still feel that the NSQIP rest pain/tissue loss variable may be lacking sensitivity in identifying the entire critical limb ischemia patient population; the strikingly similar baseline characteristics and results obtained for the full and subset analyses seems to support this and suggests that even the full cohort may largely be comprised of patients with critical limb ischemia. However, the limitations of this variable should be kept in mind for future studies done with American College of Surgeons NSQIP data.

The ASA classification was introduced in the 1960s and is both well accepted and widely used for estimating perioperative risk (we again reiterate that it is perioperative safety that our study is focused on, not limb outcomes or long-term survival). ASA class has been found to be the factor most strongly predictive of perioperative risk in both vascular surgery patients[31,32] as well as general surgery patients.[33,34] Thus, we feel justified in using this as the foundation for categorizing patients as high risk. In addition, we incorporated many of the factors of the RAND Criteria for Surgical Risk (which was also used in the Open Versus Endovascular Repair trial[35]) in our definition of high risk. We did not consider any of the cardiac risk classification schemes that have been used to predict perioperative cardiac events (ie, the Goldman Index), as our

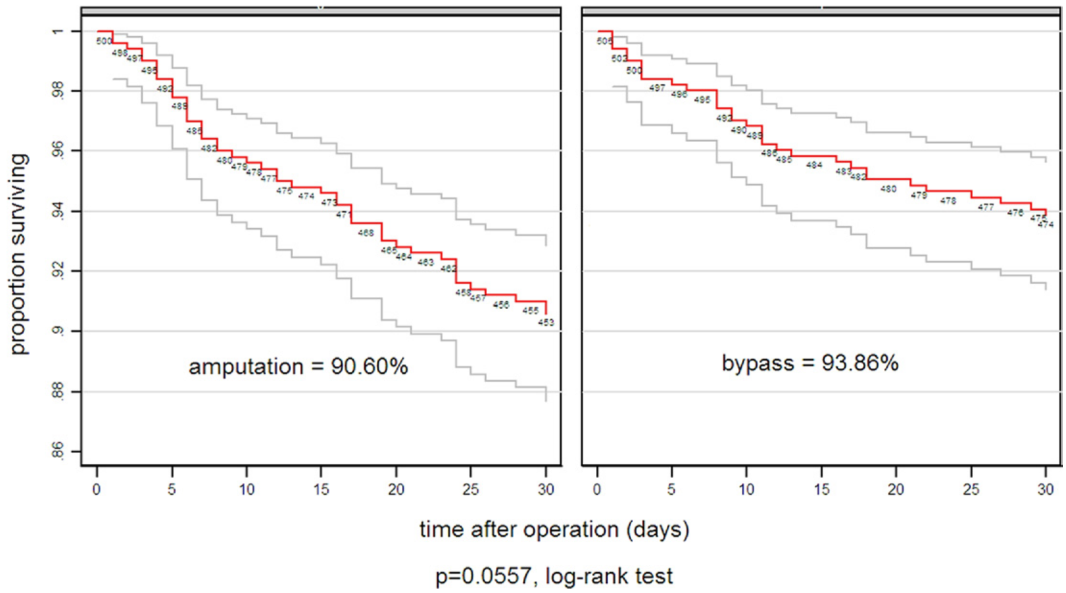

Fig 3. Kaplan-Meier product-limit estimate of 30-day postoperative mortality for high-risk, propensity score-matched subset of patients with critical limb ischemia undergoing major amputation (n = 500) or infrainguinal bypass (n = 505).

interest was overall mortality. Ultimately, any definition of risk is, to a degree, arbitrary: risk behaves more as a continuous variable (albeit in a non-linear fashion) than a categorical variable. While the 30-day survival rates of the amputation and bypass groups may change somewhat as the definition of "high-risk" changes, it would be unlikely to influence on the relative risk of mortality between the two groups and thus would not be likely to change the main findings of the study or our conclusions.

Another limitation of any nonrandomized study such as this is the potential for confounding due to unmeasured variables. For example, ankle-brachial indexes have been shown to correlate strongly with mortality,[36] but were not available to us in this study. While we have no reason to suspect that there were large differences between the ankle-brachial indexes to the amputation and bypass groups, such a difference may have existed and influenced the mortality of one group more than another. Unfortunately, there is no way to systematically eliminate the potential for such specification errors or omitted variable bias short of a randomized trial.

Finally, we do not have data on the periprocedural safety of endovascular interventions for high-risk patients such as these. A commonly held belief among vascular surgeons and interventional cardiologists seems to be that endovascular management is associated with lower morbidity and mortality. While there are no relevant studies focusing on a high-risk subset of patients, we would point to the results of the BASIL trial that demonstrated low periprocedural morbidity and mortality rates that did not differ significantly between angioplasty and surgical bypass for a general population of patients with severe limb ischemia.[37] That being said, it is not clear whether certain subgroups of patients undergoing surgical revascularization may be at higher risk for perioperative problems, such as patients having long operative times because of the need for creating a composite vein graft or challenging reoperative cases.

In summary, infrainguinal bypass was associated with a lower 30-day postoperative mortality than major amputation in the propensity score-matched, high-risk population of patients in this study. In patients with anatomy suitable for surgical revascularization and the potential for functional benefit, the presence of severe systemic comorbidities alone should not preclude infrainguinal bypass as an option for limb salvage.

The authors thank Grace Fracasso for help with compiling relevant Common Procedural Terminology codes for the study.

AUTHOR CONTRIBUTIONS

Conception and design: MB, NB
Analysis and interpretation: NB, CO, LN, MB
Data collection: NB
Writing the article: NB, LN, MB
Critical revision of the article: NB, LN, MM, RB, CO, MB
Final approval of the article: MB
Statistical analysis: NB
Obtained funding: Not applicable
Overall responsibility: MB

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Submitted Jul 5, 2010; accepted Nov 12, 2010.

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Appendix, online only. Common Procedural Terminology (CPT) codes used to identify study subjects

"Infrainguinal revascularization" procedures included any of the following CPT codes:

- Femoropopliteal bypass with vein, prosthetic conduit, or in situ (CPT codes 35556, 35656, or 35583).
- Femorotibial bypass with vein, prosthetic conduit, or in situ (CPT codes 35566, 35666, or 35585).
- Distal origin grafts with vein, prosthetic conduits, or in situ (CPT codes 35570, 35571, 35671, or 35587).

We did not include aortobifemoral bypass, iliofemoral bypass, femorofemoral bypass, axillofemoral bypass, or any type of endarterectomy, patch angioplasty, or profundaplasty *unless* it was done along with one of the above procedures at the same operation.

"Major amputation" procedures included any of the following CPT codes:

- Above-knee amputation (CPT codes 27590 and 27592).
- Below-knee amputation (CPT codes 27880 and 27882).

We did not include what are typically considered "minor" amputations: ray amputations, transmetatarsal amputations, Lisfranc amputations or Chopart amputations.